FALCIPARUM MALARIA - AN EXPERIENCE WITH 100 CASES

Abdus Salam Khan Gandapur, Salman A, Malik, Abdul Qayyum and Misal Khan

Clinical details and present day problems faced in 100 cases of Falciparum Malaria (FM) are reported. Eleven percent had taken chloroquine prior to reporting to us. The parasite density lacked correlation with the severity of disease. Pattern of fever varied markedly but 10% were afebrile throughout and presented only with body ache and malaise. Cerebral malaria was present in 117c patients. Jaundice was present in 187c patients. Other symptoms were vomiting 447c, severe headache 127c, pain abdomen 77c, loose motions/dysentery 117c, & cough 87c, while bleeding diathesis was present in 77c (3 meletia, 2 epistaxis, 1 bleeding gums and 1 haematuria). Severe anaemia was present in 107c of cases. Splenomegaly was present in 657c, hepatomegaly 297c and hepatosplenomegaly 217c. Congenital malaria was present in only one (17c) patient. Mild malaria patients were treated with chloroquine, while severe malaria patients were cured with quinine for 7 days. Blackwater fever was present in 27c. Patients with Blackwater fever were cured with steroids and chloroquine. 127c patients had chronic malaria. 837c of these patients presented with anaemia.

Self-medication, haphazard therapy and the slogan "Fever May Be Malaria, Take Chloroquine" can lead to problems in Falciparum Malaria. Clinical immunity and parasite strain may act as virulence factors.

INTRODUCTION

Today, malaria is a major health problem in many countries including Pakistan. Morbidity as well as mortality due to *Plasmodium falciparum* (PF) is on the increase, while drug resistance [1] is adding to the misery.

Falciparum Malaria (FM) can mimic many diseases, and challenges the acumen of even the most astute clinician. Self-medication by the patients usually in inadequate dosages of antimalarial is further complicating the issue. This indiscriminate use of chloroquine and Fansidar (pyrimethamine + sulphadoxine) alters the clinical course, decreases the peripheral parasitaemia and may lead to delay in the confirmation of diagnosis. This can also be conducive to the development and spread of chloroquine resistant strains.

ABDUS SALAM KHAN GANDAPUR, Department of Basic Medical Sciences, Gomal University, D.I. Khan.
SALMAN A MALIK, Department of Biology, Quaid- e-Azam University, Islamabad.
ABDUL QAYYUM, Pharmacy Department, University of Peshawar.
MISAL KHAN, Department of Health & Physical Education, Gomal University, D.I. Khan.
Corresponding Author: DR A S KHAN GANDAPUR.

MATERIALS AND METHODS

Clinical records of all patients (cases) of Falciparum Malaria reporting to District Head Quarters Hospital, D.I. Khan from August 1994 to February 1995 were analysed. Blood for malarial parasites (MP) was examined before the initiation of antimalarial therapy. Detailed history and signs and symptoms of patients were recorded on a special proforma. Parasite count was done against 200 leukocytes on a thick blood film in all patients.

Patients were divided into 2 groups on the basis of clinical severity. Group A (60 cases) was of patients who had mild symptoms and group B (40 cases) comprised of cases with severe symptoms like hyperpyrexia, cerebral symptoms, severe anaemia, bleeding problems, hepatic and kidney dysfunction. Haemoglobin, serum bilirubin, lactate dehydrogenase, alanine aminotransferase and fibrinogen degradation products (FDP) estimation was carried out in patients with anaemia, jaundice, hepatic and kidney dysfunction and bleeding problems. Platelet count was done only in patients with bleeding diathesis. Blood glucose was determined in all cases before the start of treatment to find the incidence of hypoglycemia. The duration of symptoms in 88 patients was between 2-30 days, while it was 3 months to 1 year in 12 cases.

RESULTS & CONCLUSIONS

In 100 cases ages ranged from 12 days to 70 years. Twenty-three cases (23%) were in the age range 1-14 years. Fifty (50%) were in the 21-50 years' age group, 2 cases were below 1 year of age and one was neonate. Sixteen patients (16%) were having hyperparasitaemia i.e. parasite count> 100,000 parasites /ul of blood. In 12 cases (12%) both trophozoites and gametocytes were seen in blood films for malarial parasites (MP), while in 2 patients (2%) only gametocytes were seen.

The geometric mean parasite count in group A was 5561 parasites /ul of blood while it was 25589 parasites /ul in group B. The parasite counts in group B differed significantly from group A ($P<0.001$). Table-1 shows the signs and symptoms of the patients. Ten patients (10%) had no fever, while 15 patients (15%) lapsed in a apyrexial spell after a short bout of fever. These patients denied having taken anti-malarial.

TABLE 1: SIGNS & SYMPTOMS IN PATIENTS WITH FM

S. No.	Signs & Symptoms	N	% age
01	Temperature	-	-
a)	Afebrile throughout	10	10
b)	Apyrexial spell	15	15
c)	103 - 105°F	10	10
d)	99 - 102°F	-	-
	Continuous	40	40
	Irregular	20	20
	Tertian	05	05
02	**Headache without cerebral symptoms**	10	10
03	Headache with cerebral symptoms	02	02
04	Neck rigidity	08	08
05	Melena	03	03
06	Pain abdomen	07	07
07	Vomiting	44	44
08	Diarrhoea / Dysentery	11	11
09	Jaundice	18	18
10	Cough	08	08
11	Severe anaemia (Hb < 7.0gm /dl)	10	10
12	Neurological sequelae	01	01
13	Splenomegaly	65	65
14	Hepatomegaly	20	20
15	Hepatosplenomegaly	21	21
16	Epistaxis	02	02
17	Bleeding Gums	01	01
18	Haematuria	01	01
19	Coma	02	02
20	Convulsions	03	03
21	Smoky urine	02	02

N = Number of patients.

Temperature was about 103°F in 10 (10%) patients. Forty patients (40%) had continuous fever. The most common symptoms in majority of patients in decreasing order were fever, body pains, vomiting, headache, loose motions and cough. Eleven patients (11 %) had features of cerebral malaria mainly in the form of coma, convulsions and neck stiffness. Seven patients (7%) presented with bleeding diathesis. Three (3 %) had frank melena, one bleeding from gums, two (2 %) were having epistaxis and one (1 %) had haematuria. Out of these 7 patients, platelet count was normal in 4 (150 - 400 x 10^9 /l) and decreased in the remaining patients (range 80 - 100 x 10^9/1).

FDP were normal in all the patients. Eighteen (18%) patients had jaundice; 2 (2%) patients presented with black water fever. They had no history of intake of anti-malarial. G6PD deficiency test was not done. Ten patients (10%) were severely anaemic (Hb<7.0 gm/dl), 4 patients had renal dysfunction (serum creatinine >3.0 mg/dl). Hypoglycemia (blood glucose < 40 mg/dl) was present in 8 patients. Neurological sequelae during 4 weeks follow' up were noticed only in one patient, in the form of lower motor neuron type of lesion. Thirty-five patients suffering from severe malaria responded well to quinine therapy for 7 days. Patients with mild malaria were treated with chloroquine, chloroquine and doxycycline, fansimef (Fansidar + mefloquine) and halofantrine in the recommended dosages. Patients having severe malaria were treated with quinine, 10 mg/kg body weight for 7 days.

DISCUSSION

Falciparum malaria is a syndrome and as such is a disease of protean clinical manifestations. Unscientific and presumptive treatment without proper follow up may

further worsen the situation by altering the clinical course and decreasing the number of peripheral

parasites for confirmation of diagnosis. Again the lack of skilled malaria microscopists and laboratory technicians in under developed countries may aggravate the situation. Moreover, during an epidemic, frequent chloroquine administration without radical cure and other anti-malarial measures, can exert considerable selection pressure and it can be conducive to occurrence and spread of drug resistance [2].

Self-medication and quackery result in inappropriate chloroquine administration in a significant number of patients. In our series 11 patients (11%) had taken chloroquine, prior to seeking medical advice. These patients were not relieved of symptoms, hence could be investigated, diagnosed and treated adequately. Such patients, even if cured temporarily or permanently by the presumptive treatment are the source of dissemination of PF for 2 to 3 months i.e. till the presence of gametocytes which are not killed by chloroquine / Fansidar. This hypothesis is strengthened by the fact that 14% of our patients had gametocytes in their blood film.

Sixteen percent of our patients had hyperparasitaemia. Fifty percent of these patients laid clinical jaundice, 2 (12.5%) kidney dysfunction, 5 (31%) liver dysfunction, 2 (12.5%) anaemia and 2 (12.5%) had hypoglycemia. In majority of patients with these complications, the parasite count was low. This explains the lack of correlation between severity of disease and parasite counts as observed in our series.

PF lives mainly in the visceral blood vessels and this accounts for hour to hour variation in peripheral parasitaemia. Visceral events with lethal consequences may not be paralleled by the density of parasites in the peripheral blood. Again the stage of parasite development is considered as a virulence factor in producing severity of the disease. In most of our patients, mostly tiny rings and young trophozoites of PF were seen in the peripheral blood. Silamut and White[3] demonstrated that at any stage of parasitaemia, the prognosis is worse if the parasites are mature. Moreover, a single sample for parasitic count as done by us, is insensitive because of the speed of multiplication of PF which can result in 20-fold increase in parasite count over a period of 48 hours [4].

FM presents with rather gradual onset with low grade fever which may be continuous or occur with daily spikes [5]. Moreover, during early stages, the symptoms in *Plasmodium falciparum* infection are mostly less distressing to the patient and it is usually mistaken for influenza Asymptomatic malaria without fever (latent malaria) is an occasional phenomenon in hyper endemic areas, but in our series 10 (10%) cases were afebrile. High infection rates with low prevalence

of disease has already been reported in a rural Punjabi community in Pakistan [7]. These cases had nonspecific symptoms like easy fatigability, giddiness, feeling unwell, and in some of them MP was detected on routine blood test or while being investigated for anaemia. It might be due to mild strain of PF or tolerance and immunity to parasites.

In 12 patients in our series the duration of symptoms was prolonged ranging from 3 months to 1 year. These patients gave histories of repeated attacks of PF infection. Such patients are labelled to be suffering from Chronic Falciparum Malaria. Prolonged duration of illness (5-120 days) in Falciparum malaria patients has also been reported by Abdur Rashid [8] and coworkers in the same province. Eighty-three percent of these patients presented with anaemia.

In 33% of our patients FDP levels were elevated, however, they were not of any pathological significance. The same observations have been made by Purkrittayakamee [9]. The FDP elevation in our series was not associated with cerebral malaria as reported by other workers [9,10] .

Nine patients in our study with severe malaria had hypoglycemia (blood glucose <40mg/dl). The samples were taken from the patients before quinine administration. Higher incidence of hypoglycemia has been reported by workers in other geographical areas of the world [1, 12, 13]. None of the patients with cerebral malaria in our series had hypoglycemia, as reported by other workers [n]. All of our patients with

hypoglycemia were conscious and without neurologic manifestations. This may be due to the fact that the illness in our series was less severe as compared with other series. Since chloroquine resistance has been reported in Pakistan [1], all the patients having severe malaria were treated with quinine in a dose of 10 mg/kg body weight. All the patients responded well to quinine.

To conclude, the tropical physician should always remember the protean manifestations of PF malaria. The level of parasitaemia may not correlate with disease severity. The strain and genetic polymorphism of *Plasmodium falciparum* may also act as a virulence factor. Again the clinical immunity and tolerance to parasitaemia has a role in protection against the disease particularly in endemic areas.

Indiscriminate use of present and future anti-malarial has to be avoided. Judicious combinations of presently available drugs will certainly help to overcome the problem of drug resistance till the more potent recent antimalarial like quinghaosu derivatives (i.e. artemether, sodium artesunate or artemether) are made available to us. The efforts for the development of new antimalarial by the researchers needs to be continued.

REFERENCES

1. Strickland GT & Mohyudditi MAZ. Malaria in the Punjab. Pak J Med Res. 1985, 24; 2: 49-52.
2. Anand N. In proceedings of the Indo-UK workshop on malaria, New Delhi, Nov 14-19, 1983. Malaria Research Centre (ICMR) 1984; 144-67.
3. Silamut K & White NJ. Relation of stages of parasite development in peripheral blood to prognosis in severe Falciparum malaria. Trans Roy Soc Trop Med Hyg. 1993; 87: 436-43.
4. Ellis CJ. Diagnosis not to be missed - malaria. J Applied Med. 1982; 12: 987-89.
5. Maegraith BG. In Woodruff AW. (Ed). Medicine in the tropics, London: Churchill Livingstone. 1974; 27-30.
6. Shute PG & Maryon M. Imported malaria in United Kingdom. Br Med J. 1969; 2: 781-85.
7. Khaliq AA, Fox E, Strickland GT, Latif AZ & Chaudhry MA. Malaria in rural Punjabi community: high infection rates with low prevalence of disease. Pak J Med Res 1985, 24; 2: 69-74.
8. Rashid A, Ahmad A & Roghami MT. Falciparum malaria in children. JPMA 1988, 38; 10: 268-71.
9. Purkrittayakamee S, White NJ, Clemens R, Chittamas S, Karges HE & Desakam U. Activation of coagulation cascade in Falciparum malaria. Trans Roy Soc Trop Med Hyg. 1989; 83: 762-66.
10. Vesama NJ. Intravascular coagulation in Falciparum malaria. Lancet 1972; 29: 221-23.
11. Taylor TE, Wirirna JJ, Molyneux ME. Hypoglycemia and cerebral malaria. Lancet 1990; 336: 950-52.
12. Saeed BO, Atabami GS, Nawaf A & Abdullah M et al. Hypoglycemia in pregnant women with cerebral malaria. Trans Roy Soc Trop Med Hyg. 1990; 84: 349-50.
13. Krishna S, Waller DW, Kuile FT, Kwiatkowski D & White NJ et al. Lactic acidosis and hypoglycemia in children with severe malaria - pathophysiological and prognostic significance. Trans Roy Soc Trop Med Hyg 1994; 88: 67-72.